

Microsponges: An Overview

*Hamid Hussain, Divya Juyal, Archana Dhyani

Himalayan Institute of Pharmacy and Research Rajawali Dehradun, India

Available Online: 29th September 2014

ABSTRACT

Microsponge and Nanosponge delivery System was originally developed for topical delivery of drugs can also be used for controlled oral delivery of drugs using water soluble and bioerodible polymers. Microsponge delivery system (MDS) can entrap wide range of drugs and then release them onto the skin over a time by diffusion mechanism to the skin. It is a unique technology for the controlled release of topical agents and consists of nano or micro porous beads loaded with active agent and also use for oral delivery of drugs using bioerodible polymers.

Keywords: Microsponge delivery system (MDS), Nanosponge. Bioerodible.

INTRODUCTION

Microparticles and nanoparticles have been increasingly investigated to achieve targeted and sustained release of drugs [1] and among this microsponge is one of the recent and an innovative novel approach to deliver a drug in a controlled way.

They are tiny, sponge like spherical particles that consist of a myriad of interconnecting voids within a non-collapsible structure with a large porous surface. Microsponge delivery systems (MDS) that can precisely control the release rates or target drugs to a specific body site have an enormous impact on the health care system. The microsponge drug delivery technology is widely applicable to the dermatological drug delivery products. But MDS also expands its application in oral drug delivery, bone and tissue engineering, in Detecting the diseases and in RNAi silencing. New classes of pharmaceuticals, biopharmaceuticals (peptides, proteins and DNA-based therapeutics) are fueling the rapid evolution of drug delivery technology. Thus MDS is a very emerging field which is needed to be explored [2]. Microsponges are porous, polymeric microspheres that are mostly used for prolonged topical administration. Microsponges are designed to deliver a pharmaceutically active ingredient efficiently at minimum dose and also to enhance stability, reduce side effects, and modify drug release profiles [3]. It is a polymeric microspheres that acquire the flexibility to entrap a wide variety of active ingredients such as emollients, fragrances, sunscreens, essential oils, anti-infective, anti-fungal and anti-inflammatory agents etc and are used as a topical carrier system [4]. Resembling a true sponge, each microsphere consists of an innumerable of interconnecting voids within a non-collapsible structure with a large porous surface. It is a unique technology for the controlled release of topical agents which consists of microporous beads normally 10-25 microns in diameter, loaded with active ingredients that is subsequently releases them onto the skin over a time in a controlled manner or in

response to triggers including rubbing, pH, friction, moisture and ambient skin temperature [5].

Advantages of microsponges:

- Microsponges are biologically safe and offer unique advantage of programmable release.
- They offer entrapment of numerous ingredients and is believed to contribute elegance and enhanced formulation flexibility.
- Have the capacity to adsorb or load a high degree of active materials into the particle or onto its surface.
- Microsponges are stable over a pH range of 1-11 and upto temperature of 130 °C
- They are self sterilizing as average pore size is 0.25 µm where bacteria cannot penetrate.
- Microsponges are capable of absorbing skin secretions so reducing the oiliness of the skin upto 6 times of its weight.
- With size 10-25 microns in diameter it is capable of entrapping the various ingredients in a single microsphere.
- The drug releases in microsponges by the external stimuli like pH, temperature, and rubbing.
- Microsponges have several advantages over topical preparations in being non-allergic, non-toxic, non-irritant and non-mutagenic.
- Microsponges are all ways stable i.e, thermal, physical and chemical [6].
- These are compatible with the majority of vehicles and ingredients.
- These systems have higher payload up to 50 to 60% [5].

Advantages of Microsponges over Other Formulations

Microsponges have several other advantages over other preparations available in the market. Comparison between some of them are given below as such;

Advantages over conventional formulations: Conventional formulations of topical drugs are intended to work on the

outer layers of the skin. Such products release their active

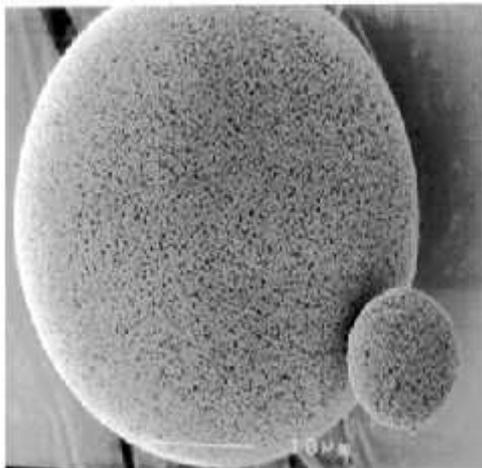


Fig. 1: View of microsponge

ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly adsorbed. When compared to the conventional system. Microsponge system can prevent excessive accumulation of ingredient within the epidermis and the dermis. Potentially, the MDDS can reduce significantly the irritation of effective drugs without reducing their efficacy. Advantages over microencapsulations and liposomes: The MDS has advantages over other technologies like microencapsulations and liposomes. Microcapsules cannot usually control the release rate of actives. Once the wall is ruptured, the actives contained within microcapsules will be released.

Liposomes suffer from lower payload, difficult formulation, limited chemical stability and microbial instability, while microsponges system in contrast to the above system has several advantages like stable over a pH range of 1-11 and upto temperature of 130 °c, stable thermally, physically and chemically, have higher payload up to 50 to 60%, have average pore size is 0.25 µm where bacteria cannot penetrate[7].

Advantages over ointments: Ointments are often aesthetically unappealing, greasiness; stickiness etc. That often results into lack of patient compliance. These vehicles require high concentrations of active agents for effective therapy because of their low efficiency of delivery system, resulting into irritation and allergic reactions in significant users. Other drawbacks of topical formulations are uncontrolled evaporation of active ingredient, unpleasant odor and potential incompatibility of drugs with the vehicles, when microsponge system maximize amount of time that an active ingredient is present either on skin surface or within the epidermis, while minimizing its transdermal penetration into the body. [8].

Characters of Drugs to be entrapped in the Microsponges: There are certain requirements that should be fulfilled (or considered) when active ingredients are entrapped into microsponge

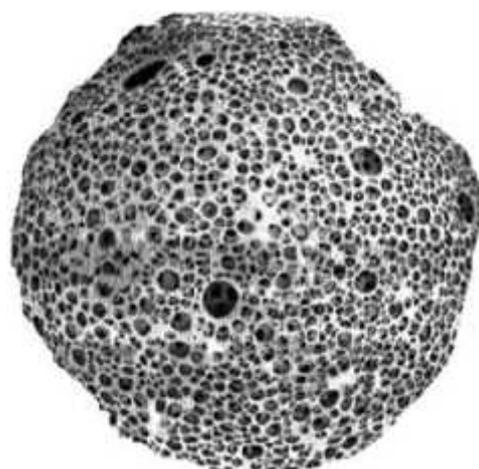


Fig. 2: Highly porous nature of a Microsponge

- It should exhibit complete miscibility in monomer or have the ability to be miscible using the least amount of a water immiscible solvent.
- Must be inert to monomers and do not increase the viscosity of the preparation during formulation.
- It should be water immiscible or almost slightly soluble.
- The solubility of active ingredients in the vehicle should be minimum; otherwise the microsponge will be diminished by the vehicle before application.
- It should maintain (preserve) the spherical structure of microsponge.
- It should be stable in polymerization conditions.
- Only 10 to 12% w/w microsponge can be incorporated into the vehicle to eliminate cosmetic delinquent.
- Payload and polymer design of the microsponges for the active must be adjusted to obtain the desired release rate of a given period of time. [9].

Methods of preparation for microsponges: Initially, drug loading in microsponges is mainly take place in two ways depending upon the physicochemical properties of drug to be loaded. If the drug is typically an inert non-polar material which will generate the porous structure then, it is known as porogen. A Porogen drug neither hinders the polymerization process nor become activated by it and also it is stable to free radicals is entrapped with one-step process (liquid-liquid suspension polymerization). Microsponges are suitably prepared by the following methods: [5]

Liquid-liquid suspension polymerization: The porous microspheres are prepared by suspension polymerization method in liquid-liquid systems. In their preparation, the monomers are first dissolved along with active ingredients in a suitable solvent solution of monomer and are then dispersed in the aqueous phase, which consist of additives (surfactant, suspend-ing agents, etc. to aid in formation of suspension). The polymerization is then initiated by adding catalyst or by increasing temperature or irradiation. The various steps in the preparation of microsponges are summarized as.

- Selection of monomer or combination of mono-mers.

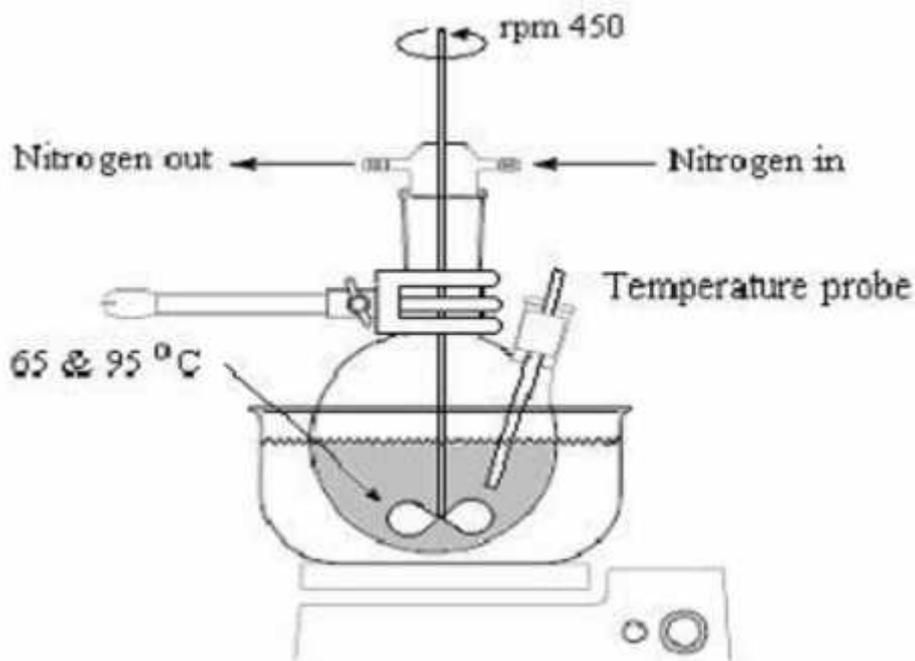


Fig 3: Instrument set up for suspension polymerization technique

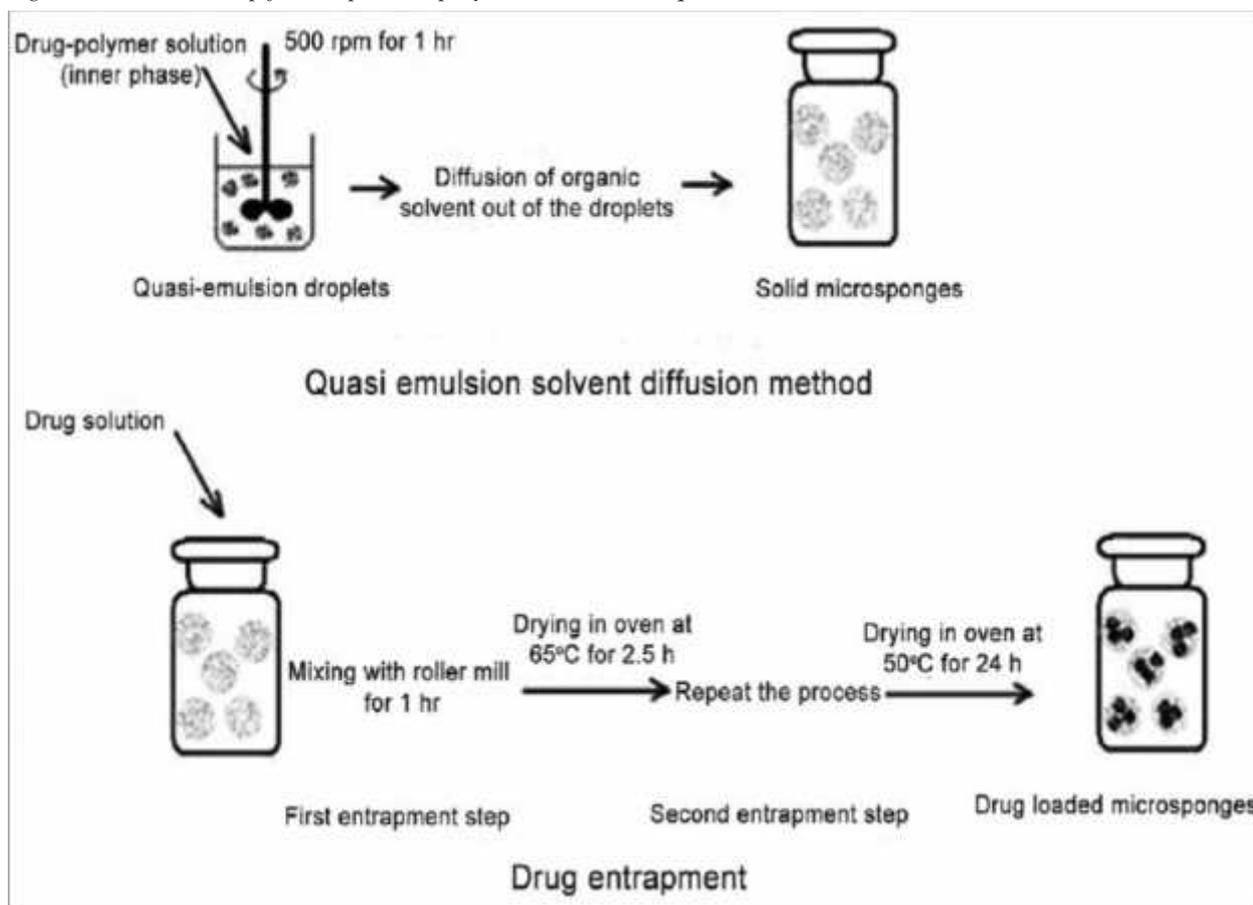


Fig 4: Quasi-emulsion solvent diffusion method set up.

- Formation of chain monomers as polymerization begins.
- Formation of ladders as a result of cross linking between chain monomers.
- Folding of monomer ladder to form spherical particles.
- Agglomeration of microspheres, which give rise to formation of bunches of microspheres.

- Binding of bunches to form microsponges. [10]

Quasi-emulsion solvent diffusion method: (Top down approach): This is top-down approach starting with preformed polymer. This process involved formation of quasi-emulsion of two different phases i.e. internal phase

and external phase similar to emulsions. The internal phase of drug--polymer solution made in a volatile solvent like ethanol or acetone or dichloromethane was added to external phase comprising the aqueous polyvinyl alcohol (PVA) solution with vigorous stirring. Triethylcitrate (TEC), which was added at an adequate amount in order to facilitate plasticity. Stirring lead to the formation of discrete emulsion globules called quasi-emulsion globules. Solvent was then extracted out from these globules to form insoluble, rigid microparticles i.e. microsponges. Following sufficient stirring, the mixture was then filtered to separate the microsponges. The microsponges were then dried in an air heated oven. Conceptually, the finely dispersed droplets of the polymeric solution of the drug(dispersed phase) get solidified in aqueous phase via counter diffusion of organic solvent and water out of and into the droplets. The diffused aqueous phase within the droplets decreased the drug and polymer solubility resulting in the co-precipitation of both the components and continued diffusion of the organic phase results in further solidification, producing matrix-type porous microspheres. In comparison with liquid--liquid suspension polymerization method, this method offered the advantage of less exposure of the drug to the ambient conditions, low solvent residues in the product because the solvent get extracted out due to its solubility in aqueous media or due to its volatile nature. [11,12,13]

Evaluation Parameters

Particle size and size distribution: Particle size and size distribution are evaluated using either an optical microscope or an electron microscope. This is an extremely crucial step, as the size of the particles greatly affects the texture of the formulation and its stability. Free-flowing powders with fine aesthetic attributes are possible to obtain by controlling the size of particles during polymerization. Particle size analysis of loaded and unloaded Microsponges can be performed by laser light diffractometry or any other suitable method. The values (d50) can be expressed for all formulations as mean size range. Cumulative percentage drug release from Microsponges of different particle size will be plotted against time to study effect of particle size on drug release. [14].

Morphology and Surface topography of SPM: For morphology and surface topography, various techniques have been used like photon correlation spectroscopy (PCS), Scanning electron microscopy (SEM), transmission electron microscopy (TEM) etc. SEM is used widely for which prepared Microsponges are coated with gold--palladium under an argon atmosphere at room temperature and then the surface morphology of the Microsponges is studied. [15].

Determination of loading efficiency and production yield: The loading efficiency (%) of the Microsponges can be calculated according to the following equation:

The production yield of the microparticles can be determined by calculating accurately the initial weight of the raw materials and the last weight of the SPM obtained. [16].

Determination of true density: The true density of Microsponges can be measured using an ultra-pycnometer under helium gas and is calculated from a mean of repeated determinations.

Pore structure: Porosity parameters of microsponges are essential in monitoring the intensity and the duration of active ingredient effect. Average pore diameters, shape and morphology of the pores can be determined by using mercury intrusion porosimetry technique. The effect of pore diameter and volume on the rate of drug release from microsponges can also be studied using the same technique. [17].

Compatibility studies: The drug-excipient compatibility studies are carried out in order to ensure that there is no inadvertent reaction between the two when formulated into a dosage form. These studies are commonly carried out by recording the differential scanning calorimetry (DSC) of both the chemicals viz., API and excipient individually and also together and checking for any addition or deletion of any peaks or troughs. For DSC approximately 5 mg samples can be accurately weighed into aluminium pans and sealed and can be run at a heating rate of 15°C/min over a temperature range 25–430°C in atmosphere of nitrogen. [18,19].

Infrared (IR) spectroscopy can also reveal the incompatibilities between the chemical moieties. Compatibility of drug with reaction adjuncts can also be studied by thin layer chromatography (TLC) and FT-IR [35]Effect of polymerization on crystallinity of the drug can be studied by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC). [20].

Polymer/ Monomer composition: Factors such as particle size, drug loading, and polymer composition govern the drug release from Microsponges. Polymer composition of the Microsponges Drug Delivery system can affect partition coefficient of the entrapped drug between the vehicle and the Microsponges system and hence have direct influence on the release rate of entrapped drug. Release of drug from Microsponge systems of different polymer compositions can be studied by plotting cumulative % drug release against time. Release rate and total amount of drug released from the system composed of methyl methacrylate/ ethylene glycol dimethacrylate is slower than styrene/divinyl benzene system. Selection of monomer is dictated both by characteristics of active ingredient ultimately to be entrapped and by the vehicle into which it will be dispersed. Polymers with varying electrical charges or degrees of hydrophobicity or lipophilicity may be prepared to provide flexibility in the release of active ingredients. Various monomer combinations will be screened for their suitability with the drugs by studying their drug release profile. [21].

Resiliency: Resiliency (viscoelastic properties) of Microsponges can be modified to produce beadlets that is softer or firmer according to the needs of the final formulation. Increased cross-linking tends to slow down the rate of release. Hence resiliency of Microsponges is studied and optimized as per the requirement by considering release as a function of crosslinking with time [22].

Table 1: Marketed formulations of microsponges[38,39]

Product name	Manufacturer	Advantages
Carac Cream	Dermik Laboratories, Inc. Berwyn , PA 19312 USA	Carac Cream contains 0.5% fluorouracil; with 0.35% being incorporated into a patented porous microsphere consisted of methyl methacrylate / glycol dimethacrylate cross-polymer and dimethicone. Carac is a once-a-day topical prescription product for the treatment of actinic keratosis (AK) that is characterized by common pre-cancerous skin condition caused by overexposure to the sun.
Salicylic Peel 20 & 30	Biophora	Retin-A-Micro contains 0.1% and 0.04% tretinoin entrapped into a patented porous microsphere consisted of methyl methacrylate/ glycol dimethacrylate cross-polymer to enable inclusion of the active ingredient, tretinoin, in an aqueous gel. This formulation is used for the topical treatment of acne vulgaris. Salicylic acid 20%, microsphere technology has excellent exfoliation and used for stimulation of the skin for more resistant skin types or for faster results. It will considerably improve pigmentation, fine lines and acne concerns. Salicylic acid moves easily through the pores, clearing them out while reducing inflammation. This treatment effectively combats acne leaving an amazingly smooth and clear complexion.
Line Eliminator Dual Retinol Facial Treatment.	Avon	Lightweight cream with a retinol (Vitamin A) in MDS, dual-system delivers both immediate and time released wrinkle-fighting action. Clearly diminishes appearance of fine lines, wrinkles & skin discolorations associated with aging.
Retin-A-Micro	Ortho-McNeil pharmaceuticals, Inc.	Retin-A-Micro contains 0.1% and 0.04% tretinoin entrapped into a patented porous microsphere consisted of methyl methacrylate/ glycol dimethacrylate cross-polymer to enable inclusion of the active ingredient, tretinoin, in an aqueous gel. This formulation is used for the topical treatment of acne vulgaris.
Micro Peel Plus /Acne Peel	Biomedic	The MicroPeel ® Plus procedure stimulates cell turnover through the application of salicylic acid in the form of microcrystals using Microsphere® technology. These microcrystals target the exact areas on the skin that need improvement. The MicroPeel Plus aggressively outperforms other superficial chemical peels by freeing the skin of all dead cells while doing no damage to the skin.
Retinol cream, Retinol 15 Night cream	Biomedic, Sothys	A night time treatment cream with Microsphere technology using a stabilized formula of pure retinol, Vitamin A. Continued use of Retinol 15 will result in the visible diminishment of fine lines and wrinkles, a noticeable improvement in the skin discolorations due to aging, and enhanced skin smoothness.
Lactrex™ 12% Moisturizing Cream	SDR Pharmaceuticals, Inc., Andover , NJ , U.S.A. 07821	Lactrex™ 12% Moisturizing Cream contains 12% lactic acid as the neutral ammonium salt, ammonium lactate. Microsphere® technology has been included for easy application and long lasting moisturization. Lactrex™ also contains water and glycerin, a natural humectant to soften and help moisturize drys, flaky, cracked skin.
EpiQuin Micro	SkinMedica Inc	The Microsphere® system uses microscopic reservoirs that entrap hydroquinone and retinol. The microspheres release these ingredients into the skin gradually throughout the day. This provides the skin with continuous exposure to hydroquinone and retinol over time, which may minimize skin irritation. EpiQuin Micro is a prescription moisturizing fading cream that reduces the impact of these conditions known as melasma, post inflammatory hyper pigmentation or solar lentigines. Also help in Age spots, Sun spots and Facial discoloration.

Table 1: Marketed formulations of microsponges[38,39]

Product name	Manufacturer	Advantages
Oil free matte block spf20	Dermalogica	This invisible oil-free sunscreen shields the skin from damaging UV sun rays while controlling oil production, giving you a healthy matte finish. Formulated with micro sponge technology, Oil free matter block absorbs oil and preventing shine without any powdery residue.
Sportscream RS and XS	Embil Pharmaceutical Co. Ltd.	Topical analgesic-anti-inflammatory and counterirritant actives in a micro sponge® delivery system (MDS) for the management of musculoskeletal conditions.
Oil Control Lotion	Fountain Cosmetics	A feature-light lotion with technically advanced microsponges that absorb oil on the skin's surface during the day, for a matte finish. Eliminate shine for hours with this feature-weight lotion, formulated with oil-absorbing Microsponge technology. The naturally- antibiotic Skin Response Complex soothes inflammation and tightness to promote healing. Acne-Prone, oily skin conditions.

Kinetics of release: To determine the drug release mechanism and to compare the release profile differences among microsponges, the drug released amount versus time was used. The release data were analysed with the following mathematical models:

$$Q = k_1 t^n \text{ or } \log Q = \log k_1 + n \log t \dots\dots\dots \text{Equation (1)}$$

Where Q is the amount of the released at time (h), n is a diffusion exponent which indicates the release mechanism, and k_1 is a constant characteristic of the drug-polymer interaction. From the slope and intercept of the plot of log Q versus log t, kinetic parameters n and k_1 were calculated. For comparison purposes, the data was also subjected to Equation (2), which may be considered a simple, Higuchi type equation.

$$Q = k_2 t^{0.5} + C \dots\dots\dots \text{Equation (2)}$$

Equation (2), for release data dependent on the square root of time, would give a straight line release profile, with k_2 presented as a root time dissolution rate constant and C as a constant. [23].

Invitro Study

In vitro release studies, release kinetics and mechanism:

In vitro release studies can be performed using United States Pharmacopeial (USP) dissolution apparatus equipped with a modified basket consisted of 5 µm stainless steel mesh at 37°C. The release medium is selected according to the type of formulation that is, topical or oral, while considering solubility of active ingredients to ensure sink conditions. Sample aliquots are withdrawn from the medium and analyzed by suitable analytical method at regular intervals of time. The drug release from topical preparations (for example, creams, lotions and emulgels) containing microsponges can be carried out using Franz diffusion cells. Dialysis membrane is fitted into place between the two chambers of the cell. A predetermined amount of formulation is mounted on the donor side of Franz cell. The receptor medium is continuously stirred at and thermostated with a circulating jacket. Samples are withdrawn at different time

intervals and analyzed using suitable method of assay (Embil and Nacht, 1996; Jelvehgari et al., 2006). To determine the drug release kinetics and investigate its mechanism from microsponges, the release data are fitted to different kinetic models. The kinetic models used are; first order, zero order, Higuchi and Korsmeyer- Peppas models (Higuchi, 1963; Wagner, 1969; Korsmeyer et al., 1983; Peppas, 1985). The goodness of fit was evaluated using the determination coefficient (R²) values. [24]

Safety Considerations

Safety studies of microsponges can be confirmed by;

- Allergenicity in guinea pigs
- Eye irritation studies in rabbits
- Mutagenicity in bacteria
- Oral toxicity studies in rats.
- Skin irritation studies in rabbits. [25,26,27]

Applications of Microsponge Systems: Microsponge delivery systems are used to enhance the safety, effectiveness and aesthetic quality of topical prescription, over-the-counter and personal care products. Products under development or in the market place utilize the Topical Microsponge systems in three primary ways:

- As reservoirs releasing active ingredients over an extended period of time,
- As receptacles for absorbing undesirable substances, such as excess skin oils, or
- As closed containers holding ingredients away from the skin for superficial action.

Releasing of active ingredients from conventional topical formulations over an extended period of time is quite difficult.

Cosmetics and skin care preparations are intended to work only on the outer layers of the skin. The typical active ingredient in conventional products is present in a relatively high concentration and, when applied to the skin, may be rapidly absorbed. The common result is over-medication, followed by a period of under-medication until the next application. Rashes and more serious side effects can occur when the active ingredients rapidly penetrate below the skin's surface. Microsponge technology is

designed to allow a prolonged rate of release of the active ingredients, thereby offering potential reduction in the side effects while maintaining the therapeutic efficacy. [28].

Microsponge for topical delivery: The Microsponge systems are based on microscopic, polymer-based microspheres that can bind, suspend or entrap a wide variety of substances and then be incorporated into a formulated product, such as a gel, cream, liquid or powder. A single Microsponge is as tiny as a particle of talcum powder, measuring less than one-thousandth of an inch in diameter. Like a true sponge, each microsphere consists of a myriad of interconnecting voids within a non-collapsible structure that can accept a wide variety of substances. The outer surface is typically porous, allowing the controlled flow of substances into and out of the sphere.

Several primary characteristics, or parameters, of the Microsponge system can be defined during the production phase to obtain spheres that are tailored to specific product applications and vehicle compatibility. Microsponge systems are made of biologically inert polymers. Extensive safety studies have demonstrated that the polymers are non-irritating, nonmutagenic, non-allergenic, non-toxic and non-biodegradable. As a result, the human body cannot convert them into other substances or break them down. Although they are microscopic in size, these systems are too large to pass through the stratum corneum when incorporated into topical products [29]. Benzoyl peroxide (BPO) is commonly used in topical formulations for the treatment of acne, with skin irritation as a common side effect. It has been shown that controlled release of BPO from a delivery system to the skin could reduce the side effect while reducing percutaneous absorption. Therefore, microsponge delivery of Benzoyl peroxide was developed using an emulsion solvent diffusion method by adding an organic internal phase containing benzoyl peroxide, ethyl cellulose and dichloromethane into a stirred aqueous phase containing polyvinyl alcohol and by suspension polymerization of styrene and divinyl benzene. The prepared microsponges were dispersed in gel base and microsponge gels are evaluated for anti-bacterial and skin irritancy. The entrapped system released the drug at slower rate than the system containing free BPO. Topical delivery system with reduced irritancy was successfully developed. [30,31,32]

Microsponge for oral delivery: In oral applications, the microsponge system has been shown to increase the rate of solubilization of poorly water-soluble drugs by entrapping such drugs in the microsponge system's pores. As these pores are very small, the drug is in effect reduced to microscopic particles and the significant increase in the surface area thus greatly increases the rate of solubilization. Controlled oral delivery of ibuprofen microsponges is achieved with an acrylic polymer, Eudragit RS, by changing their intraparticle density. Sustained release formulation of chlorpheniramine maleate, using powder-coated microsponges, is prepared by the dry impact blending method, for oral drug delivery. Controlled oral delivery of Ketoprofen prepared by quasi-emulsion solvent diffusion method with Eudragit RS 100 and afterwards tablets of

microsponges were prepared by the direct compression method. Results indicated that compressibility was much improved in the physical mixture of the drug and polymer; due to the plastic deformation of the sponge-like microsponge structure, producing mechanically strong tablets. Colon-specific, controlled delivery of flurbiprofen was conducted by using a commercial Microsponge® 5640 system. *In vitro* studies exhibited that compression-coated colon-specific tablet formulations started to release the drug at the eighth hour, corresponding to the proximal colon arrival time, due to addition of the enzyme, following a modified release pattern, while the drug release from the colon-specific formulations prepared by pore plugging the microsponges showed an increase at the eighth hour, which was the point of time when the enzyme addition was made. [33,34].

Microsponge for Bone and Tissue Engineering: Bone-substitute compounds were obtained by mixing pre-polymerized powders of polymethylmethacrylate and liquid methylmethacrylate monomer with two aqueous dispersions of tricalcium phosphate grains and calcium deficient hydroxyapatite powders. The final composites appeared to be porous and acted as microsponges. Basic fibroblast growth factor (bFGF) incorporated in a collagen sponge sheet was sustained released in the mouse sub-cutis according to the biodegradation of the sponge matrix, and exhibited local angiogenic activity in a dose-dependent manner. The injection of collagen microsponges incorporating bFGF induced a significant increase in the blood flow, in the murine ischemic hind limb, which could never have been attained by the bolus injection of bFGF. These results suggest the significance and therapeutic utility of the type I collagen as a reservoir of bFGF. [35,36]

Future Prospects: Microsponge drug delivery system holds a promising opportunity in various pharmaceutical applications in the upcoming future as it has unique properties like enhanced product performance and elegance, extended release, improved drug release profile, reduced irritation, improved physical, chemical and thermal stability which makes it flexible to develop novel product forms. The real challenge in future is the development of the delivery system for the oral peptide delivery by varying ratio of polymers. The use of bioerodible and biodegradable polymers for the drug delivery is enabling it for the safe delivery of the active material. As these porous systems have also been studied for the drug delivery through pulmonary route which shows that these system can show effective drug release even in the scarce of the dissolution fluid thus colon is an effective site for targeting for drug release. These carriers also require to be developed for alternative drug administration routes like parenteral and pulmonary route. These particles can also be used as the cell culture media and thus can also be employed for stem cell culture and cellular regeneration in the body. Due to their elegance, these carrier systems have also found their application in cosmetics. These developments enabled researchers to utilize them variably. These novelties in formulation also open new ways for drug delivery. [37]

CONCLUSION

MDS has become highly competitive and rapidly evolving technology and more and more research are carrying out to optimize cost-effectiveness and efficacy of the therapy. It is a unique technology for the controlled release of topical agents and consists of microporous beads loaded with active agent and also use for oral as well as biopharmaceutical drug delivery. Microsponge delivery systems that can precisely control the release rates or target drugs to a specific body site have a vast impact on the health care system. A microsponge delivery system can release its active ingredient on a time mode and also in response to other stimuli. Therefore, microsponge has got a lot of potential and is a very emerging field which is needed to be explored. Microsponges constitute a significant part by virtue of their small size and efficient carrier characteristics.

REFERENCES

- De-Jalon EG, Blanco-Prieto MJ, Ygartua P, Santoyo S. Topical application of acyclovir-loaded microparticles: quantification of the drug in porcine skin layers. *J Control Release*. (2001) 191–7.
- Ramadevi Bhimavarapu, Ramesetti RamaDevi, Srinath Nissankararao, Chaitanya Devarapalli, Sowjanya Paparaju. Microsponges: As a Novel Imperative for Drug Delivery System. *RJPT*: (August 2013)
- Orlu M, Cevher E, Araman A. Design and evaluation of colon specific drug delivery system containing flubiprofen microsponges. *Int J Pharm*. (2006) 318:103–17.
- Embil K, Nacht S, The microsponge delivery system (MDS): A topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives, *J Microencapsul*, 13, (1996) 575-588.
- Jain Neelam, Kumar Sharma Pramod, Banik Arunabha. **RECENT ADVANCES IN MIROSPONGES DRUG DELIVERY SYSTEM**. , *IJPSRR*: (May – June 2011) 13-14
- Gangadharappa, H.V; vishal Gupta N.; Chandra Prasad M., Sara; Shivakumar, H.G. Current trends in Microsponge drug delivery system.
- N.H palookar, A.S kulkarni, D.J Ingale and R.A patil. Microsponges as innovative drug delivery system. *IJPSN* volume 5. issue 1. (April-june 2012) 1600-1601
- Saroj Kumar Pradhan: microsponges as the versatile tool for drug delivery system
- Hibah Aldawsari1 and Shaimaa M. Badr-Eldin. Microsponges as promising vehicle for drug delivery and targeting: Preparation, characterization and Applications. *AJPP* (2013) 875
- Viral Shaha, Hitesh Jain1, Jethva Krishna1, Prमित Patel. Microsponge drug delivery: A Review. *IJRPS* (2010) 213
- Jelvehgari M, Siahi-Shadbad MR, Azarmi S, Gary P, Martin, Nokhodchi A: The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies. *International Journal of Pharmaceutics* (2006)124-132.
- Kawashima Y, Niwa T, Takeuchi H, Hino T, Ito Y. Control of Prolonged Drug Release and Compression Properties of Ibuprofen Microsponges with Acrylic Polymer, Eudragit RS, by Changing Their Intraparticle Porosity. *Chemical and pharmaceutical bulletin*. (1992) 196-201
- Comoglu T, Gonul N, Baykara T. Preparation and in vitro evaluation of modified release ketoprofen microsponges. *Il Farmaco*. (2003) 101-6.
- Martin A., Swarbrick J., Cammarrata A. In: *Physical Pharmacy- Physical Chemical Principles in Pharmaceutical Sciences*. 3rd Ed. (1991) 527
- Emanuele A.D., Dinarvand R. Preparation, characterization and drug release from thermoresponsive microspheres. *Int.Journal of Pharmaceutics*. (1995) 237-242.
- Kilicarslan M, Baykara T. The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres. *Int. J. Pharm*. (2003) 99–109.
- Hibah Aldawsari1 and Shaimaa M. Badr-Eldin. Microsponges as promising vehicle for drug delivery and targeting: Preparation, characterization and Applications. *AJPP* (8 May, 2013) 876
- Jones D.S., Pearce K.J. Investigation of the effects of some process variables on microencapsulation of propranolol HCl by solvent evaporation method. *Int J. Pharm* (1995) 99-205.
- Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y, Furuyama S. Characterization of polymorphs of tranilast anhydrate and tranilast monohydrate when crystallized by two solvent change spherical crystallization techniques. *J. Pharm. Sci*. (1991) 472-478.
- Ford J.L., Timmins P. *Pharmaceutical Thermal Analysis- Techniques and Applications*. Ellis Horwood Ltd.: Chichester. (1989)
- Chowdary KPR, Rao Y.S. Mucoadhesive Microspheres for Controlled Drug Delivery. *Biol. Pharm. Bull* .(2004) 1717- 1724.
- Peppas N.A., Analysis of Fickian and non-Fickian drug release from polymers. *Pharm. Acta Helv*. (1985) 110–111.
- Hibah Aldawsari1 and Shaimaa M. Badr-Eldin. Microsponges as promising vehicle for drug delivery and targeting: Preparation, characterization and Applications. *AJPP* (8 May, 2013) 877
- Sato T., Kanke M., Schroeder G., Deluca P. Porous biodegradable microspheres for controlled drug delivery. Assessment of processing conditions and solvent removal techniques. *Pharm Res*. (1988) 21-30.
- Kilicarslan M, Baykara T. The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres. *Int. J. Pharm*. (2003) 99–109.

26. Draize J.H., Woodard G., Calvery H.O. Methods for the study of irritation and toxicity of substances applied topically to the Skin and Mucous Membranes. *J Pharmacol Exp Ther.* (1944) 377-389.
27. Saraf A., Dasani A., Pathan H., Microsponge drug delivery system as an innovation in Cosmetic world A Review. *Asian Journal of Pharmaceutical Education and Research*, (2012) 2278 – 7496
28. Patel G., Patel J., Use of a Microsponge in Drug Delivery Systems, *Pharmaceutical processing*, (2008) 158
29. D'souza JI. In-vitro Antibacterial and Skin Irritation Studies of Microsponges of Benzoyl Peroxide. *Indian Drugs*. (2001) 23.
30. Wester R., Patel R., Natch S., Leyden J., Melendres J., Maibach H., Controlled release of benzoyl peroxide from a porous microsphere polymeric system can reduce topical irritancy, *J. Am. Acad. Derm.*, (1991) 720-726.
31. John I. D'souza, Jagdish K. Saboji, Suresh G. Killedar, Harinath N. More "Design and Evaluation of Benzoyl Peroxide Microsponges to Enhance Therapeutic Efficacy in Acne Treatment", Accepted for presentation in 20th FAPA Congress, Bangkok, Thailand, (Nov 30- Dec 3, 2004
32. Jain V., Singh R., Dicyclomine-loaded eudragit based microsponge with potential for colonic delivery Preparation and characterization. *Tropical Journal of Pharmaceutical Research*, (2010) 67-72
33. Mine Orlu, Erdal Cevher, Ahmet Araman Design and evaluation of colon specific drug delivery system containing flurbiprofen microsponges, *International Journal of Pharmaceutics*, (2006) 103–117.
34. Shaheen S Z, Bolla K, Vasu K & Singara C M A. Antimicrobial activity of the fruit extracts of *Coccinia indica*. *African Journal of Biotechnology* Vol. 8(24) (2009) 7073-7076
35. Park W H, Lee S J and Moon H I. Antimalarial Activity of a New Stilbene Glycoside from *Parthenocissus tricuspidata* in Mice. *Antimicrobial Agents and Chemotherapy*. 52(9) (2008): 3451–3453.
36. Srivastava R, Pathak K. Microsponges: a futuristic approach for oral drug delivery. *Expert Opin. Drug Deliv.*, (2012) 863-878.
37. Embil VP, OTC external analgesic cream/topical analgesic anti-inflammatory, counterirritant utilizing the microsponge delivery system (MDS) for controlled release of actives, UK Patent 01010586, 2000.
38. Grimee PE, Meraz M, A new microentrapped 4% hydroquinone formulation for treatment of hyperpigmentation, 60th Annual meeting of American Academy of Dermatology. (2002) 22-27.